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SPONASTRIME Dysplasia: Report on a Female Patient With Severe Skeletal Changes

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We report on a 6-year-old girl with SPONASTRIME dysplasia, characterized by short-limbed dwarfism, a relatively large head, midfacial hypoplasia, a saddle nose, moderate deformities of the vertebral bodies, striated metaphyses, and normal intelligence. She showed severe skeletal changes including marked delay of epiphyseal ossification, evident metaphyseal dysplasia, and osteopathia striata more pronounced than in most of the previously reported patients with this disorder. The patient we describe and a male patient reported by Camera et al. [1994: Pediatr Radiol 24:322–324] are likely to represent the severely-affected end of the clinical spectrum of the disorder. These findings thus rule out the X-linked mode of inheritance of the disorder proposed by Camera et al. [1994: Pediatr Radiol 24: 322–324]. Alternatively, the two severely-affected patients may represent a variant form of the disorder. There is evidence that SPONASTRIME dysplasia is a genetically heterogeneous disorder. © 1996 Wiley-Liss, Inc.

KEY WORDS: SPONASTRIME dysplasia, genetic heterogeneity, autosomal-recessive inheritance, laryngotracheomalacia, subglottic stenosis

INTRODUCTION

SPONASTRIME dysplasia (MIM 271510) is a rare genetic disorder characterized by short-limbed dwarfism, moderate deformities of the vertebral bodies, striated metaphyses, midfacial hypoplasia, and relative macrocephaly. The designation of the disorder, SPONASTRIME dysplasia, was derived from *spo*ndylar and *na*sal alterations with *stri*ation of the *me*taphyses [Fanconi et al., 1983]. Nine patients, 7 girls and 2 boys, in four families have been described. Autosomal-recessive inheritance has been suggested [Fanconi et al., 1983; Lachman et al., 1989; Camera et al., 1993; Verloes et al., 1995]. On the other hand, X-linked inheritance has been proposed based on a male patient with more severe skeletal changes than those observed in female patients [Camera et al., 1994]. We herein describe a girl affected by SPONASTRIME dysplasia with severe skeletal changes. The inheritance pattern and classification of SPONASTRIME dysplasia are discussed.

CLINICAL REPORT

The patient, a girl, was the first child of healthy nonconsanguineous Japanese parents. The mother was age 28 and the father age 29 at the time of her birth. They had a healthy son 3 years later. The mother had no history of abortions or stillbirths. Her height was 158 cm (mean), and the father's was 171 cm (mean). Labor was induced 5 days after term due to premature rupture of the membranes and weak contractions. At birth, the patient weighed 2,650 g, her length was 48.0 cm, and her occipito-frontal circumference (OFC) was 31.0 cm. She had mild neonatal asphyxia. She has been hospitalized several times since age 6 months for recurrent episodes of dyspnea due to laryngotracheomalacia and subglottic stenosis with associated upper respiratory infections. She sat alone at age 8 months and walked unaided at 19 months. She spoke meaningful words at 18 months.

She was first evaluated at age 16 months because of short stature. Her height was 66.0 cm (−4.4 SD), weight 7.7 kg (−1.9 SD), and OFC 45.3 cm (−0.4 SD). She had frontal bossing, hypertelorism, a low nasal bridge with a depressed tip, a hypoplastic columella, short nose with anteverted nostrils, protuberant upper lip, and downturned corners of the mouth (Fig. 1). Also noted were mild mesomelic shortening of the lower extremities, hypermobile wrists, and limited extension of the elbow joints. Genu valgum has been progressive

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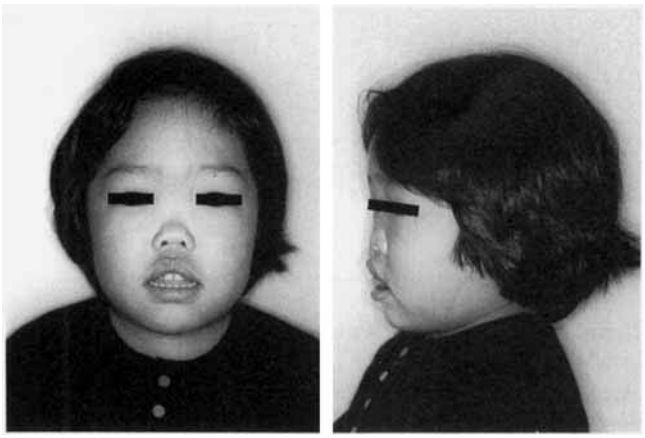

Fig. 1 Patient at age 4 years.

since age 5 years. Now at age 6 years, her height is 94.2 cm (−4.1 SD), weight 16.1 kg (−1.4 SD), and OFC 51.0 cm (mean). Psychomotor development is normal. She has normal chromosomes. Other normal laboratory tests include insulin-like growth factor 1, serum chemistries, amino acids, immunoglobulins, complete blood counts, and urinalysis. Growth hormone (GH) secretion, assessed by pharmacological stimulation tests and GH concentrations during sleep, is normal (clonidine test: GH peak, 8.9 ng/ml; insulin test: 5.6 ng/ml; mean GH concentration during sleep: 7.3 ng/ml). Serum thyroid hormone and urine 17-OHCS are normal. The luteinizing hormone (LH)-releasing hormone stimulation test disclose a hyperresponse of follicle-stimulating hormone. Ultrasound examination of the abdomen show a hypoplastic uterus, a finding suggestive of primary ovarian hypofunction. It is surmised, however, that this is not the case, considering the normal LH response and normal ultrasound findings of the ovaries.

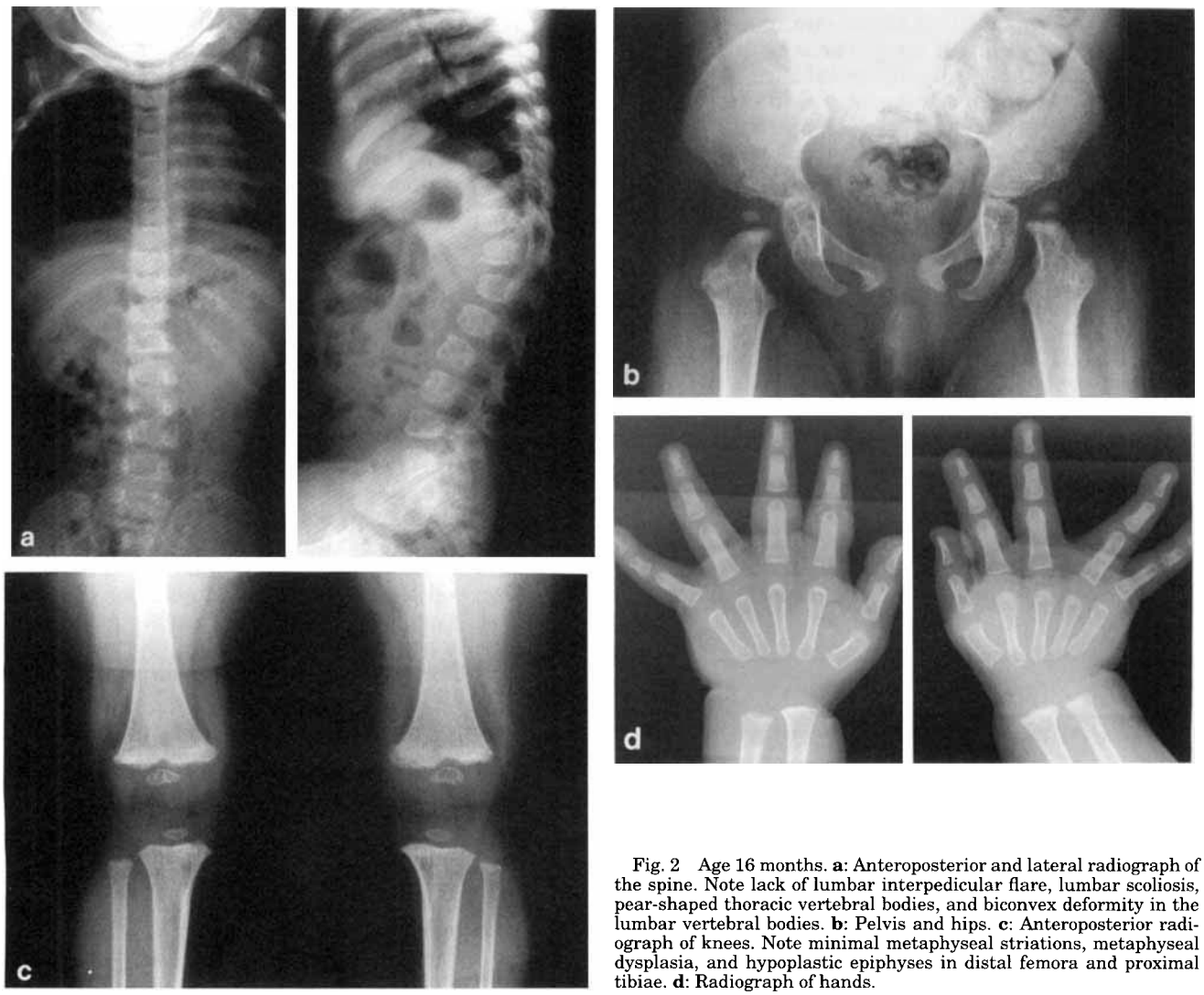

Fig. 2 Age 16 months. **a**: Anteroposterior and lateral radiograph of the spine. Note lack of lumbar interpedicular flare, lumbar scoliosis, pear-shaped thoracic vertebral bodies, and biconvex deformity in the lumbar vertebral bodies. **b**: Pelvis and hips. **c**: Anteroposterior radiograph of knees. Note minimal metaphyseal striations, metaphyseal dysplasia, and hypoplastic epiphyses in distal femora and proximal tibiae. **d**: Radiograph of hands.

Radiographic Changes

Two skeletal surveys were performed, the first at age 16 months and the second at age 6 years. Abnormal findings at the first survey included mild dolichocephaly with frontal bossing, a barrel-shaped chest, pear-shaped thoracic vertebral bodies, asymmetric primary ossification and biconvex deformity of the lumbar vertebral bodies, and narrowing of the interpediculate distance of the lower lumbar spine with concavities of the posterior vertebral bodies. Thoracolumbar kyphosis and lumbosacral lordosis were exaggerated (Fig. 2a). The proximal femora appeared markedly constricted, with coxa valga (Fig. 2b). Minimal longitudinal striations were seen in the distal femoral and proximal tibial metaphyses. The metaphyseal ends were flared and irregular. The epiphyses of the knees were small (Fig. 2c). The proximal radial heads were hypoplastic and posteriorly subluxed. The carpal ossification centers and epiphyseal ossification of the short tubular bones were not seen (Fig. 2d). The survey at age 6 years showed deformities of the thoracolumbar vertebral bodies, the same as in the first survey, and in addition, irregular endplates. Minimal platyspondyly of the upper lumbar spine was evident on frontal view, while on side view, posterior scalloping of the vertebral bodies gave rise to the appearance of "tall vertebrae" (Fig. 3a). The iliac crests demonstrated a crenated appearance (Fig. 3b). Metaphyseal striations were more pronounced than before, involving the distal femora and the proximal tibiae. Metaphyseal irregularity was more pro-

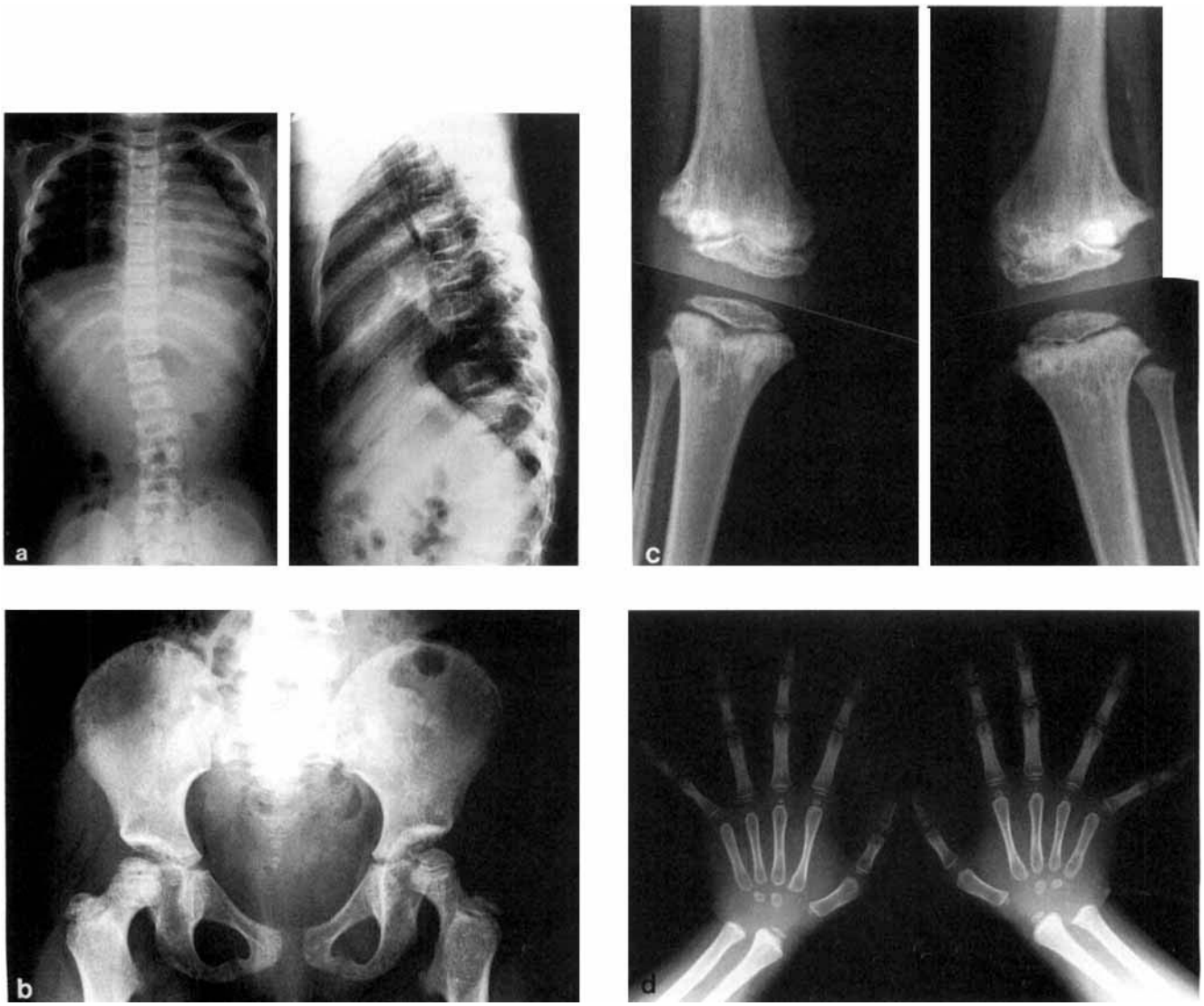

Fig. 3 Age 6 years. **a**: Anteroposterior and lateral radiograph of spine. Note indentations on the superior and inferior aspects of the vertebral endplates. **b**: Pelvis and femora. **c**: Anteroposterior radiograph of knees. Note markedly delayed epiphyseal ossification, evident metaphyseal dysplasia, and dense metaphyseal striations. **d**: Radiograph of hands.

nounced in the knees. The epiphyses of the knees were markedly flattened. Genu valgum was substantial (Fig. 3c). Distal metaphyseal striations of the radii were noted. Bone age of the hand was significantly retarded at 15 months, according to the method of Greulich-Pyle [1959] (Fig. 3d).

DISCUSSION

The clinical manifestations in the 6-year-old girl we describe support the diagnosis of SPONASTRIME dysplasia. She had short-limbed dwarfism, relative macrocephaly, frontal bossing, midface hypoplasia, a saddle nose, and normal intelligence. Her skeletal changes were more pronounced than those usually seen in patients with this disorder. She showed severe skeletal changes including marked delay of epiphyseal ossification, evident metaphyseal dysplasia, and metaphyseal striation of the long bones much more marked than in most previously reported patients.

Autosomal-recessive inheritance of the disorder has been suggested by the description of three sets of affected sibs, 7 girls and 1 boy age 2–18 years, born to normal parents [Fanconi et al., 1983; Lachman et al., 1989; Camera et al., 1993]. On the other hand, an X-linked mode of inheritance has been proposed based on a 5-year-old boy with severe skeletal changes comparable to the girl we describe [Camera et al., 1994]. X-linked inheritance of the disorder is unlikely in view of the fact that both male and female patients can be severely affected. The patient we describe and the male reported on by Camera et al. [1994] are likely to represent the severely-affected end of the clinical spectrum of the disorder. Alternatively, these 2 patients may represent a variant entity similar to, but different from, SPONASTRIME dysplasia.

A variant form of SPONASTRIME dysplasia was recently reported, with microcephaly and mental retardation [Camera et al., 1993; Verloes et al., 1995]. We have seen 2 patients with another variant of this disorder, with characteristic facies, craniosynostosis, and bulbous dorsum sellae [Nishimura et al., submitted]. These findings point to possible genetic heterogeneity.

The laryngotracheomalacia and subglottic stenosis in the present patient, which have not been described in the previously reported patients with SPONASTRIME dysplasia, expand the phenotype of the disorder.

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